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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	NOV 21	CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS	3	NOV 26	MARPAT enhanced with FSORT command
NEWS	4	NOV 26	CHEMSAFE now available on STN Easy
NEWS	5	NOV 26	Two new SET commands increase convenience of STN searching
NEWS	6	DEC 01	ChemPort single article sales feature unavailable
NEWS	7	DEC 12	GBFULL now offers single source for full-text coverage of complete UK patent families
NEWS	8	DEC 17	Fifty-one pharmaceutical ingredients added to PS
NEWS	9	JAN 06	The retention policy for unread STNmail messages will change in 2009 for STN-Columbus and STN-Tokyo
NEWS	10	JAN 07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data
NEWS	11	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS	12	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS	13	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS	14	FEB 10	COMPENDEX reloaded and enhanced
NEWS	15	FEB 11	WTEXTILES reloaded and enhanced
NEWS	16	FEB 19	New patent-examiner citations in 300,000 CA/CAplus patent records provide insights into related prior art
NEWS	17	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS	18	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS	19	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS	20	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS	21	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:18:39 ON 24 FEB 2009

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 10:19:02 ON 24 FEB 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 FEB 2009 HIGHEST RN 1110296-20-2
DICTIONARY FILE UPDATES: 22 FEB 2009 HIGHEST RN 1110296-20-2

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

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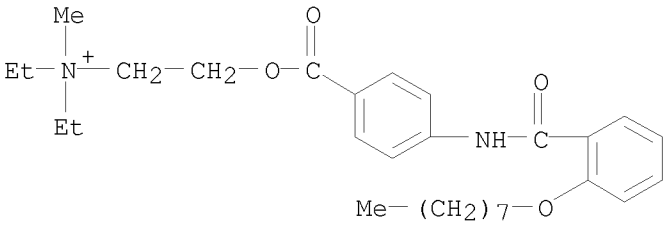
http://www.cas.org/support/stngen/stndoc/properties.html

=> s octylonium bromide
```
             1 OCTYLONIUM
        189620 BROMIDE
            30 BROMIDES
        189620 BROMIDE
                  (BROMIDE OR BROMIDES)
L1           1 OCTYLONIUM BROMIDE
                  (OCTYLONIUM(W)BROMIDE)
```

=> d L1 str cn rn

L1 ANSWER 1 OF 1 REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Ethanaminium, N,N-diethyl-N-methyl-2-[[4-[[2-(octyloxy)benzoyl]amino]benzoyl]oxy]-, bromide (1:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ammonium, diethyl(2-hydroxyethyl)methyl-, bromide, p-[o-(octyloxy)benzamido]benzoate (8CI)
CN Benzoic acid, p-[o-(octyloxy)benzamido]-, ester with diethyl(2-hydroxyethyl)methylammonium bromide (8CI)
CN Ethanaminium, N,N-diethyl-N-methyl-2-[[4-[[2-(octyloxy)benzoyl]amino]benzoyl]oxy]-, bromide (9CI)
OTHER NAMES:
CN Octylonium bromide
CN Otilonium bromide
CN SP 63
CN Spasmomen
RN 26095-59-0 REGISTRY

=> file caplus medline biosis embase

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.71	13.93

FILE 'CAPLUS' ENTERED AT 10:20:07 ON 24 FEB 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'MEDLINE' ENTERED AT 10:20:07 ON 24 FEB 2009

FILE 'BIOSIS' ENTERED AT 10:20:07 ON 24 FEB 2009

FILE 'EMBASE' ENTERED AT 10:20:07 ON 24 FEB 2009

=> s L1
L2 334 L1

=> s octylonium bromide
L3 111 OCTYLONIUM BROMIDE

=> s 26095-59-0
L4 334 26095-59-0

```
=> s L2 or L3 or L4
L5         349 L2 OR L3 OR L4

=> dup rem L5
PROCESSING COMPLETED FOR L5
L6          215 DUP REM L5 (134 DUPLICATES REMOVED)

=> s anticancer drug
L7       41671 ANTICANCER DRUG

=> s L6 and L7
L8           1 L6 AND L7

=> s L6 and drug
L9         170 L6 AND DRUG

=> s tablet or capsule
L10     399380 TABLET OR CAPSULE

=> s L6 and L10
L11         18 L6 AND L10

=> d L8 ibib abs

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2004:80493  CAPLUS
DOCUMENT NUMBER:         140:122743
TITLE:                   P-glycoprotein inhibitor comprising octilonium bromide
                         as an effective ingredient
INVENTOR(S):             Chung, Hesson; Jeong, Seo-young; Kwon, Ick-chan; Park,
                         Yeong-taek; Lee, In-hyun; Yuk, Soon-hong
PATENT ASSIGNEE(S):      Korea Institute of Science and Technology, S. Korea
SOURCE:                  PCT Int. Appl., 33 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004009073         A1    20040129    WO 2003-KR1441          20030721
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     KR 2004009018         A     20040131    KR 2002-42794           20020720
     AU 2003281468         A1    20040209    AU 2003-281468          20030721
     EP 1545495            A1    20050629    EP 2003-741600          20030721
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     US 20060141033        A1    20060629    US 2005-521678          20050902
PRIORITY APPLN. INFO.:                       KR 2002-42794        A  20020720
                                             WO 2003-KR1441       W  20030721
AB   The invention relates to a new use of octylonium bromide
     as p-glycoprotein inhibitor to increase cellular uptake of drugs.  More
```

particularly, the invention provides octylonium bromide as a p-glycoprotein inhibitor to increase cellular uptake of drugs such as anticancer drugs by taking octylonium bromide simultaneously with or proceeding drug administration.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d L11 1-18 ibib abs

L11 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:116839 CAPLUS
TITLE: Preparation of substituted cyclohexanol derivatives for use as opioid receptor modulators
INVENTOR(S): Gant, Thomas G.; Sarshar, Sepehr
PATENT ASSIGNEE(S): Auspex Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 54pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20090028873	A1	20090129	US 2008-180421	20080725
WO 2009018169	A1	20090205	WO 2008-US71251	20080725

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2007-952292P P 20070727
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and II [X = C(R1)2N[C(R1)3]2; each R1 independently = H or D; R23 = H, CH3, D, CDH2, CD2H, or CD3; provided that at least one R1 is D or R23 is D, CDH2, CD2H, or CD3], and their pharmaceutically acceptable salts, are prepared and disclosed as opioid receptor modulators. Thus, e.g., III•HCl was prepared by methoxylation of 3-bromophenol with d3-iodomethane followed by a Grignard reaction with 2-(dimethylaminomethyl)cyclohexanone (preparation given), and resolution
Select I
and II were evaluated in human liver microsomal (HLM) stability (in vitro) assays, e.g., III demonstrated a 50-150% increase of HLM degradation half-life. I and II were disclosed as opioid receptor modulators and/or neurotransmitter reuptake modulators.

L11 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1190255 CAPLUS

DOCUMENT NUMBER: 147:491589
TITLE: Otilonium bromide capsule for treating irritable bowel syndrome or gastrospasm
INVENTOR(S): Zhang, Ming
PATENT ASSIGNEE(S): Beijing Dezhong Wangquan Medicine Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 10pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 101053562	A	20071017	CN 2006-10073074	20060412

PRIORITY APPLN. INFO.: CN 2006-10073074 20060412

AB The title capsule contains otilonium bromide 5-100 mg, and has a dissoln. rate in vitro of over 90 % within 5 min. The capsule may also comprise disintegrating agent selected from crosslinked PVP, low-substituted hydroxypropyl cellulose, crosslinked sodium CM-cellulose and sodium carboxymethyl starch, bulking agent selected from lactose, starch, dextrin, sugar and microcryst. cellulose, and lubricant selected from magnesium stearate, stearic acid, calcium stearate and silicon dioxide. The capsule can be used for treating irritable bowel syndrome or gastrospasm.

L11 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:457122 CAPLUS
DOCUMENT NUMBER: 146:468993
TITLE: Determination of otilonium bromide and its related substances in otilonium bromide tablets by HPLC
AUTHOR(S): Zhao, Tie; Li, Zhong; Li, Yuan; He, Zhonggui
CORPORATE SOURCE: Department of Pharmacy, Affiliated Second Hospital, China Medical University, Shenyang, 110004, Peop. Rep. China
SOURCE: Huaxi Yaoxue Zazhi (2006), 21(6), 583-584 CODEN: HYZAE2; ISSN: 1006-0103
PUBLISHER: Huaxi Yike Daxue Yaoxueyuan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The content and related substances of otilonium bromide tablets were determined by HPLC with Diamonsil (ODS-C18) column (200 mm + 4.6 mm, 5 μm). The mobile phase was sodium acetate trihydrate buffer(0.3 mol/L) containing 3 mmol/L heptanesulfonic acid monohydrate sodium mixed-acetonitrile-methanol(30:70:20, pH6.0). The detective wavelength was 293 nm. The excipients did not interfere with the determination of otilonium bromide.

Otilonium bromide and its related substance could be completely separated The linear range of otilonium bromide was 10-100 μg/mL with RSD of 0.5%, and the average recovery was 100.3%. The method is simple, accurate, and specific. It can be used for the content determination and examination of the related substances in otilonium bromide tablets.

L11 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:201307 CAPLUS
DOCUMENT NUMBER: 146:236179
TITLE: Therapeutic compositions and methods for treating colon diseases
INVENTOR(S): Del Soldato, Piero

PATENT ASSIGNEE(S): CTG Pharma S.r.l., Italy
SOURCE: PCT Int. Appl., 26pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007019888	A2	20070222	WO 2006-EP2783	20060327
WO 2007019888	A3	20070712		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: EP 2005-425598 A 20050812

AB Compns. containing mesalamine or its derivs. and a co-agent effective for the treatment of gastrointestinal altered motility, sensitivity and secretion and abdominal viscera disorders including both functional and organic diseases are useful for the treatment of irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). Furthermore the present invention provides formulations and methods for treating IBS and IBD. Tablets contained mesalazine 600.00, dicyclomine-HCl 20.00, lactose monohydrate 130.00 sodium starch glycolate 25.00, Povidone 9.00, Mg stearate 6.00, and talc 10.00 mg.

L11 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1316108 CAPLUS
DOCUMENT NUMBER: 144:94224
TITLE: Preparation of traditional Chinese medicines for treating intestinal dysfunction
INVENTOR(S): Yang, Xinghao
PATENT ASSIGNEE(S): Nanjing Normal University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 36 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1579485	A	20050216	CN 2004-10014337	20040316

PRIORITY APPLN. INFO.: CN 2004-10014337 20040316

AB The basic formula of the traditional Chinese medicine for treating intestinal dysfunction contains Bupleurum 6-18 g, Paeonia lactiflora 6-30 g, Pseudostellaria heterophylla 3-18 g, and Glycyrrhiza 6-15 g. The basic formula can be used directly or is used to prepare extract The extraction process comprises: (1) extracting volatile oil from above materials, (2) collecting the residues, extracting with water, ethanol, or other organic solvents to get a solution, vacuum-concentrating, precipitating with ethanol, purifying with absorbent resin

and exchange resin, centrifuging at high speed, and coating with cyclodextrin, and (3) mixing the extract coated with cyclodextrin with above volatile oil to get the final product. Following materials or their exts. may be added: Atractylodes macrocephala, Ligusticum chuanxiong, Poria cocos, Pueraria, Uncaria, Citrus aurantium. Compds. such as smecta and domperidone can also be added. The preparation method of the composition is also
provided in the invention.

L11 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:80493 CAPLUS
DOCUMENT NUMBER: 140:122743
TITLE: P-glycoprotein inhibitor comprising octilonium bromide as an effective ingredient
INVENTOR(S): Chung, Hesson; Jeong, Seo-young; Kwon, Ick-chan; Park, Yeong-taek; Lee, In-hyun; Yuk, Soon-hong
PATENT ASSIGNEE(S): Korea Institute of Science and Technology, S. Korea
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009073	A1	20040129	WO 2003-KR1441	20030721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2004009018	A	20040131	KR 2002-42794	20020720
AU 2003281468	A1	20040209	AU 2003-281468	20030721
EP 1545495	A1	20050629	EP 2003-741600	20030721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060141033	A1	20060629	US 2005-521678	20050902
PRIORITY APPLN. INFO.:			KR 2002-42794 A	20020720
			WO 2003-KR1441 W	20030721

AB The invention relates to a new use of octylonium bromide as p-glycoprotein inhibitor to increase cellular uptake of drugs. More particularly, the invention provides octylonium bromide as a p-glycoprotein inhibitor to increase cellular uptake of drugs such as anticancer drugs by taking octylonium bromide simultaneously with or proceeding drug administration.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:745483 CAPLUS
DOCUMENT NUMBER: 136:139972
TITLE: Optimization and validation of a capillary electrophoresis method for the simultaneous determination of diazepam and otilonium bromide
AUTHOR(S): Furlanetto, Sandra; Orlandini, Serena; Massolini, Gabriella; Faucci, Maria Teresa; La Porta, Enzo;

Pinzauti, Sergio
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Florence, Florence, 50121, Italy
SOURCE: Analyst (Cambridge, United Kingdom) (2001), 126(10), 1700-1706
CODEN: ANALAO; ISSN: 0003-2654
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simultaneous assay of diazepam and otilonium bromide in coated tablets by capillary zone electrophoresis (CZE) was developed. The influence of various parameters (voltage, temperature, buffer concentration and pH, ethanol percent) on anal. time and on the theor. plates of the 2 peaks was investigated by means of exptl. design. A response surface study was carried out by means of a 27-run D-optimal matrix. The best background electrolyte was 0.13 M, and the pH 2.9 Britton-Robinson buffer containing 10% EtOH. Other optimized parameters were voltage (30 kV) and temperature (30°). The UV detector for quantitation of otilonium bromide and diazepam was set at 280 and 230 nm, resp. Procaine hydrochloride was used as internal standard and the run time was <5 min. Validation was performed for the drug and the drug product, according to ICH3 guidelines. For the drug product, the recovery for otilonium bromide and diazepam ranged from 98.3 to 101.2% and from 97.1 to 99.0%, resp.; the RSD values found for otilonium bromide and diazepam ranged from 2.4 to 3.0% and from 1.1 to 4.5%, resp.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:900422 CAPLUS
DOCUMENT NUMBER: 134:61524
TITLE: Controlled-release and taste-masking oral compositions
INVENTOR(S): Villa, Roberto; Pedrani, Massimo; Ajani, Mauro; Fossati, Lorenzo
PATENT ASSIGNEE(S): Cip-Ninety Two-92 S.A., Panama
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076478	A1	20001221	WO 2000-EP5356	20000609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 99MI1317	A1	20001214	IT 1999-MI1317	19990614
IT 2000MI0422	A1	20010903	IT 2000-MI422	20000303
IT 1317871	B1	20030715		
CA 2377301	A1	20001221	CA 2000-2377301	20000609
EP 1183014	A1	20020306	EP 2000-942044	20000609
EP 1183014	B1	20031008		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

TR 200200562	T2	20020521	TR 2002-562		20000609
JP 2003501457	T	20030114	JP 2001-502812		20000609
AT 251449	T	20031015	AT 2000-942044		20000609
PT 1183014	T	20031231	PT 2000-942044		20000609
ES 2208349	T3	20040616	ES 2000-942044		20000609
CN 1173695	C	20041103	CN 2000-808894		20000609
RU 2246293	C2	20050220	RU 2002-100367		20000609
IN 2001DN01113	A	20050311	IN 2001-DN1113		20011203
US 7431943	B1	20081007	US 2001-9532		20011212
MX 2001012889	A	20030624	MX 2001-12889		20011213
NO 2001006108	A	20020124	NO 2001-6108		20011214
IN 2001DN01163	A	20080912	IN 2001-DN1163		20011218
HK 1046244	A1	20050603	HK 2002-107843		20021030
US 20060134208	A1	20060622	US 2005-268500		20051108
US 7410651	B2	20080812			
US 20060159749	A1	20060720	US 2006-378378		20060320
US 7410652	B2	20080812			
US 20090011010	A1	20090108	US 2008-210969		20080915
PRIORITY APPLN. INFO.:			IT 1999-MI1317	A	19990614
			IT 2000-MI422	A	20000303
			WO 2000-EP5356	W	20000609
			US 2001-9532	A2	20011212
			US 2005-262799	A2	20051101

AB This invention relates to controlled release and taste masking compns. containing one or more active principles incorporated in a three-component matrix structure, i.e. a structure formed by amphiphilic, lipophilic or inert matrixes and finally incorporated or dispersed in hydrophilic matrixes. The use of a plurality of systems for the control of the dissoln. of the active ingredient modulates the dissoln. rate of the active ingredient in aqueous and/or biol. fluids, thereby controlling the release kinetics in the gastrointestinal tract. For example, a taste-masked buccal tablet contained ibuprofen 100, cetyl alc. (lipophilic/inert matrix) 15, soy lecithin (amphiphilic matrix) 8, mannitol (hydrophilic matrix) 167, maltodextrin 150, hydroxypropyl Me cellulose 30, aspartame 15, flavors 5, colloidal silica 5, and Mg stearate 5 mg.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:736903 CAPLUS

DOCUMENT NUMBER: 134:9418

TITLE: Development and validation of a near infrared method for the analytical control of a pharmaceutical preparation in three steps of the manufacturing process

AUTHOR(S): Blanco, M.; Coello, J.; Iturriaga, H.; Maspoch, S.; Pou, N.

CORPORATE SOURCE: Facultat de Ciencies, Unitat de Quimica Analitica, Departament de Quimica, Universitat Autonoma de Barcelona, Bellaterra, 08193, Spain

SOURCE: Fresenius' Journal of Analytical Chemistry (2000), 368(5), 534-539
CODEN: FJACES; ISSN: 0937-0633

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A near IR diffuse reflectance spectroscopy (NIRS) procedure for the quant. control anal. of the active compound (otilonium bromide) in a pharmaceutical preparation in three steps of the production process (blended product, cores and coated tablets) and a methodol. for its validation are proposed.

The anal. procedure is composed by two consecutive steps. First, the sample is identified by comparing its spectrum with a second derivative spectral library. If the sample is pos. identified, the active compound is quantified by using a previously established partial least squares (PLS) calibration model. The procedure was validated by studying repeatability, intermediate precision, accuracy and linearity. To this end, an adaptation of ICH (International Conference on Harmonization) validation methodol. to an NIR multivariate calibration procedure is proposed. The relative standard error of prediction (RSEP) was ≤ 1% and the suitability of the procedure for control anal. was confirmed by the results obtained analyzing new production samples produced over a three-month period.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:456321 CAPLUS
DOCUMENT NUMBER: 119:56321
ORIGINAL REFERENCE NO.: 119:10021a,10024a
TITLE: High-performance liquid chromatographic method for assay of otilonium bromide, diazepam, and related compounds in finished pharmaceutical forms
AUTHOR(S): Mannucci, Carlo; Bertini, Jacopo; Cocchini, Aldo; Perico, Andrea; Salvagnini, Franco; Triolo, Antonio
CORPORATE SOURCE: Anal. Res. Dep., A. Menarini Ind. Farm. Riunite s.r.l., Florence, 50131, Italy
SOURCE: Journal of Pharmaceutical Sciences (1993), 82(4), 367-70
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A rapid, simple, stability-indicating assay procedure for otilonium bromide, a smooth muscle relaxant agent, and diazepam in composite tablet anal. was developed with HPLC. The tablet matrix was dissolved with water, and drugs were extracted with acetonitrile containing an internal standard An aliquot was centrifuged and chromatographed on a 5-μm, reversed-phase column with 0.5 M sodium acetate trihydrate buffer containing 5 mM 1-heptanesulfonic acid monohydrate sodium salt:methanol (30:70; volume/volume; adjusted to pH 6.0 with acetic acid) as the mobile phase. The selectivity of the chromatog. system was demonstrated by resolving both compds. from various potential degradation products of each compound The method is linear, quant., and reproducible.

L11 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:27592 CAPLUS
DOCUMENT NUMBER: 118:27592
ORIGINAL REFERENCE NO.: 118:4993a,4996a
TITLE: Simultaneous determination of otilonium bromide and diazepam by first-derivative spectroscopy
AUTHOR(S): Mannucci, Carlo; Bertini, Jacopo; Cocchini, Aldo; Perico, Andrea; Salvagnini, Franco; Triolo, Antonio
CORPORATE SOURCE: Anal. Res. Dep., A. Menarini Ind. Farm. Riunite S.r.l., Florence, 50131, Italy
SOURCE: Journal of Pharmaceutical Sciences (1992), 81(12), 1175-7
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A rapid, simple assay procedure was developed for simultaneous anal. of otilonium bromide, a smooth-muscle relaxant, and diazepam in tablets containing 20 mg of otilonium bromide and 2 mg diazepam (20:2

tablets) or 40 mg otilonium bromide and 2 mg diazepam (40:2 tablets) by "zero-crossing" first-derivative spectrophotometry. The tablets were dissolved in 0.01 N HCl, mixts. were centrifuged at 3500 rpm for 5 min, and first-deriv spectra were recorded. The absolute values of the derivative were measured at 264 nm for determination of otilonium bromide and between 406 and 408 nm (380 nm for anal. of 40:2 tablets) for determination of diazepam. The method is linear, quant., and reproducible and can also be used for the tablet dissoln. test. Ten tablets of the same batch were analyzed by the above method and by HPLC, and the results were in good agreement.

L11 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:457298 CAPLUS
DOCUMENT NUMBER: 115:57298
ORIGINAL REFERENCE NO.: 115:9777a,9780a
TITLE: Simultaneous determination of otilonium bromide and diazepam by high-performance liquid chromatography
AUTHOR(S): Santoni, G.; Fabbri, L.; Mura, P.; Renzi, G.; Gratteri, P.; Pinzauti, S.
CORPORATE SOURCE: Stabil. Chim. Farm. Mil., Florence, Italy
SOURCE: International Journal of Pharmaceutics (1991), 71(1-2), 1-5
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A reversed-phase HPLC method for the simultaneous determination of otilonium bromide and diazepam in tablets was developed. Owing to the residual free silanol groups on the modified silica surface, otilonium bromide eluted from the reversed-phase column without retardation effects, using a methanol-water eluent containing Me4NBr and HOAc. The effects of the Me4NBr concentration on the capacity and symmetry factors of otilonium bromide and diazepam were investigated.

L11 ANSWER 13 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2004568125 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15540426
TITLE: [New approaches to diagnosing and treating hyperkinetic biliary dyskinesia associated with chronic acalculous cholecystitis].
Novye podkhody k diagnostike i lecheniiu giperkineticheskikh diskinezii zhelchnogo puzyria v sochetanii s khronicheskim nakal'kuleznym kholetsistitom.
AUTHOR: Bartosh L F; Balakina I V; Gridneva L M
SOURCE: Klinicheskaia meditsina, (2004) Vol. 82, No. 9, pp. 57-9.
Journal code: 2985204R. ISSN: 0023-2149.
PUB. COUNTRY: Russia: Russian Federation
DOCUMENT TYPE: (COMPARATIVE STUDY)
(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 16 Nov 2004
Last Updated on STN: 2 Feb 2005
Entered Medline: 31 Jan 2005
AB Ninety patients aged 21 to 56 years who had chronic non-calculous cholecystitis (CNCC) concurrent with hyperkinetic dyskinesia (HKD) detectable by a stepwise duodenal probing and sonography, by using a choleretic breakfast and by determining the relaxation coefficient (RC) that was equal to the ratio of the volume of the gallbladder (GB) after the use of a spasmolytic to the baseline GB volume. The patients were divided into 3 groups. The authors used as a spasmolytic agent pinaverium

bromide (dicetel) in a dose of 50 mg (1 tablet) in Group 1), octylonium bromide (spasmomen) in a dose of 40 mg (1 dragee) in Group 2, and drotaverine (no-spa) in a dose of 40 mg (1 tablet). There was a more significant sonographic increase in the size of GB in Groups 1 and 2 as compared with Group 3. In the acute drug test and during long-term treatment as well, the highest spasmolytic effect was noted in patients receiving dicetel (Group 1) and spasmomen (Group 2) as compared with that in Group 3 patients taking drotaverine. With this, RC was 1.25 +/- 0.2, 1.6 +/- 0.15, and 1.08 +/- 0.1, respectively. No adverse reactions occurred in the patients having selective calcium blockers (SCBs) whereas the patients receiving no-spa were found to have the following side effects: dry mouth (n = 3), transient constipation (n = 1), and numb tongue (n = 1). Thus, the study has provided evidence for the fact that SCBs have some advantage over myotropic spasmolytic agents in the treatment of CNCC with the signs of HKD.

L11 ANSWER 14 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1999000904 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9784726
TITLE: [The use of Spasmomen (otilonium bromide) in pediatrics]. Primenenie spazmomena (otiloniia bromida) v pediatrii.
AUTHOR: Lasitsa O I; Revutskaia A E
SOURCE: Likars'ka sprava / Ministerstvo okhorony zdorov'ia Ukrainy, (1998 Jun) No. 4, pp. 124-7.
Journal code: 9601540. ISSN: 1019-5297.
PUB. COUNTRY: Ukraine
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 25 Nov 1998
AB Spasmomen is an affective medicinal substance for treating functional pathologies of digestive organs in children. The above drug is well tolerated, with no adverse events or complications being associated with its intake. Spasmomen as a drug having spasmolytic effect can be recommended for use in pediatric practice for treating children in all age brackets.

L11 ANSWER 15 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1993009563 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1395454
TITLE: [The otilonium bromide-benzodiazepine combination in the therapy of the irritable colon syndrome]. L'associazione ottilionio bromuro-benzodiazepina nella terapia della sindrome del colon irritabile.
AUTHOR: Capurso L; Del Sette F; Ferrario F; Tarquini M
CORPORATE SOURCE: Servizio di Gastroenterologia e Endoscopia Digestiva, Ospedale S. Filippo Neri, Roma.
SOURCE: La Clinica terapeutica, (1992 Aug) Vol. 141, No. 8, pp. 121-7.
Journal code: 0372604. ISSN: 0009-9074.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 22 Jan 1993
Last Updated on STN: 22 Jan 1993
Entered Medline: 13 Nov 1992

AB The irritable bowel syndrome is classified ad "disturbance of intestinal motility without an identifiable anatomic substrate". However, the clear etiopathogenetic implications of a psychosomatic nature complicate the search for an adequate therapeutic strategy. Based on this clinical experience, we set out to check the importance of a spasmolytic with a benzodiazepine and the tolerability of this type of combination. We therefore compared the results in 60 patients with irritable bowel syndrome of 8 weeks' treatment with tablets containing octylonium bromide (OB) 20 mg plus diazepam (DZ) 2 mg or OB 40 mg + 2 mg DZ. The doubling of the spasmolytic without increasing the daily dose of anxiolytic appeared to be useful for reducing the symptoms typical for the irritable bowel syndrome. In addition, the combination was found to be perfectly tolerated.

L11 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:32167 BIOSIS
DOCUMENT NUMBER: PREV199395020367
TITLE: Octylonium bromide plus diazepam versus diazepam or octylonium bromide alone in the treatment of irritable bowel syndrome. An open controlled clinical trial.
AUTHOR(S): Capurso, L.; Del Sette, F.; Tarquini, M.; Ferrario, F.
CORPORATE SOURCE: Service Gastroenterol. and Digestive Endoscopy, San Filippo Neri Hosp., Rome, Italy
SOURCE: Current Therapeutic Research, (1992) Vol. 52, No. 3, pp. 368-377.
CODEN: CTCEA9. ISSN: 0011-393X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Dec 1992
Last Updated on STN: 10 Feb 1993

AB The authors report the results obtained in 121 patients with irritable bowel syndrome (IBS) associated with habitual anxiety. Patients were divided into three groups treated with ocytlonium bromide 40 mg plus diazepam 2 mg (OB + D, three tablets/day) octylonium bromide 40 mg (OB, three tablets/day), or diazepam 2 mg (D, three tablets/day), respectively. In each group, treatment was continued for 3 months and was preceded by a 15-day washout with placebo. Efficacy of treatment in controlling abdominal pain symptoms and gas distension was evaluated by means of a visual analogue scale (VAS) and a visual rating scale (VRS). The OB + D combination proved effective in most treated patients, and a statistically significant difference was found (P lt 0.001) between this treatment and treatment with D alone in reducing abdominal pain intensity (87.2% mean reduction of VAS and VRS scores) and in reducing gas distension (60.3% mean reduction of VAS and VRS scores). Comparison between the combination and OB alone showed a significant difference only in reduction of abdominal pain (P lt 0.001). The anxiety symptoms associated with IBS were assessed using Zung's self-rating anxiety scale and were found to be reduced in all three patient groups after 90 days' treatment, although the reductions were more marked in patients treated with the OB + D combination and with D alone.

L11 ANSWER 17 OF 18 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2007359482 EMBASE
TITLE: Analytical methodologies for the determination of omeprazole: An overview.

AUTHOR: Espinosa Bosch, M.
CORPORATE SOURCE: Department of Pharmacy, General Hospital, University Hospital Virgen del Rocio, Manuel Siurot s/n, 41013 Sevilla, Spain.
AUTHOR: Ruiz Sanchez, A.J.
CORPORATE SOURCE: Department of Organic Chemistry, Faculty of Sciences, University of Malaga, Campus Teatinos s/n, 29071 Malaga, Spain.
AUTHOR: Sanchez Rojas, F. (correspondence); Bosch Ojeda, C.
CORPORATE SOURCE: Department of Analytical Chemistry, Faculty of Sciences, University of Malaga, Campus Teatinos s/n, 29071 Malaga, Spain. fsanchezr@uma.es
SOURCE: Journal of Pharmaceutical and Biomedical Analysis, (15 Aug 2007) Vol. 44, No. 4, pp. 831-844.
Refs: 91
ISSN: 0731-7085 CODEN: JPBADA
PUBLISHER IDENT.: S 0731-7085(07)00245-2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
039 Pharmacy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 2007
Last Updated on STN: 27 Aug 2007

AB Omeprazole, a gastric acid pump inhibitor, dose-dependently controls gastric acid secretion; the drug has greater antisecretory activity than histamine H(2)-receptor antagonists. Omeprazole has been determined in formulations and biological fluids by a variety of methods such as spectrophotometry, high-performance liquid chromatography with ultraviolet detection and liquid chromatography coupled with tandem mass spectrometry. The overview includes the most relevant analytical methodologies used in its determination since the origin still today. .COPYRGT. 2007 Elsevier B.V. All rights reserved.

L11 ANSWER 18 OF 18 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2000372428 EMBASE
TITLE: Alosetron.
AUTHOR: Mucke, H.; Cole, P.; Rabasseda, X., Dr. (correspondence)
CORPORATE SOURCE: Medical Information Department, Prous Science, P.O. Box 540, 08080 Barcelona, Spain.
SOURCE: Drugs of Today, (2000) Vol. 36, No. 9, pp. 595-607.
Refs: 48
ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2000
Last Updated on STN: 16 Nov 2000

AB Alosetron, a 5-HT(3)-receptor antagonist that is very closely related to ondansetron in terms of both chemistry and pharmacology, is the first compound of this type to be developed for irritable bowel syndrome. Clinical data for up to 3 months of treatment indicate that alosetron is

orally bioavailable in tablet form, is well tolerated and is significantly superior to both placebo and the smooth muscle relaxant, mebeverine, in improving perception of visceral pain, spasms and diarrhea in female diarrhea-predominant irritable bowel syndrome. In males, symptoms were not alleviated to a statistically significant extent. (C) 2000 Prous Science.

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=> s L6 and (AY<2003 or PY<2003 or PRY<2003)
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
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   3 FILES SEARCHED...
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'2003' NOT A VALID FIELD CODE
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=> s p-glycoprotein
L13      50229 P-GLYCOPROTEIN

=> s L6 and L13
L14          2 L6 AND L13

=> dup rem L14
PROCESSING COMPLETED FOR L14
L15           2 DUP REM L14 (0 DUPLICATES REMOVED)

=> s slow release
L16      24060 SLOW RELEASE

=> s L6 and L16
L17          0 L6 AND L16

=> s oral or subcutaneous or intravenous
L18    3008993 ORAL OR SUBCUTANEOUS OR INTRAVENOUS

=> s L6 and L18
L19         44 L6 AND L18

=> dup rem L19
PROCESSING COMPLETED FOR L19
L20          44 DUP REM L19 (0 DUPLICATES REMOVED)

=> s L20 and (AY<2003 or PY<2003 or PRY<2003)
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L21         30 L20 AND (AY<2003 OR PY<2003 OR PRY<2003)

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L21  ANSWER 1 OF 30  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2004:80493  CAPLUS
DOCUMENT NUMBER:         140:122743
TITLE:                   P-glycoprotein inhibitor comprising octilonium bromide
                         as an effective ingredient
INVENTOR(S):             Chung, Hesson; Jeong, Seo-young; Kwon, Ick-chan; Park,
```

Yeong-taek; Lee, In-hyun; Yuk, Soon-hong
PATENT ASSIGNEE(S): Korea Institute of Science and Technology, S. Korea
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009073	A1	20040129	WO 2003-KR1441	20030721 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2004009018	A	20040131	KR 2002-42794	20020720 <--
AU 2003281468	A1	20040209	AU 2003-281468	20030721 <--
EP 1545495	A1	20050629	EP 2003-741600	20030721 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060141033	A1	20060629	US 2005-521678	20050902 <--
PRIORITY APPLN. INFO.:			KR 2002-42794 A	20020720 <--
			WO 2003-KR1441 W	20030721

AB The invention relates to a new use of octylonium bromide as p-glycoprotein inhibitor to increase cellular uptake of drugs. More particularly, the invention provides octylonium bromide as a p-glycoprotein inhibitor to increase cellular uptake of drugs such as anticancer drugs by taking octylonium bromide simultaneously with or proceeding drug administration.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:900422 CAPLUS
DOCUMENT NUMBER: 134:61524
TITLE: Controlled-release and taste-masking oral compositions
INVENTOR(S): Villa, Roberto; Pedrani, Massimo; Ajani, Mauro; Fossati, Lorenzo
PATENT ASSIGNEE(S): Cip-Ninety Two-92 S.A., Panama
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076478	A1	20001221	WO 2000-EP5356	20000609 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

IT	99MI1317	A1	20001214	IT 1999-MI1317	19990614 <--
IT	2000MI0422	A1	20010903	IT 2000-MI422	20000303 <--
IT	1317871	B1	20030715		
CA	2377301	A1	20001221	CA 2000-2377301	20000609 <--
EP	1183014	A1	20020306	EP 2000-942044	20000609 <--
EP	1183014	B1	20031008		

R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

TR	200200562	T2	20020521	TR 2002-562	20000609 <--
JP	2003501457	T	20030114	JP 2001-502812	20000609 <--
AT	251449	T	20031015	AT 2000-942044	20000609 <--
PT	1183014	T	20031231	PT 2000-942044	20000609 <--
ES	2208349	T3	20040616	ES 2000-942044	20000609 <--
CN	1173695	C	20041103	CN 2000-808894	20000609 <--
RU	2246293	C2	20050220	RU 2002-100367	20000609 <--
IN	2001DN01113	A	20050311	IN 2001-DN1113	20011203 <--
US	7431943	B1	20081007	US 2001-9532	20011212 <--
MX	2001012889	A	20030624	MX 2001-12889	20011213 <--
NO	2001006108	A	20020124	NO 2001-6108	20011214 <--
IN	2001DN01163	A	20080912	IN 2001-DN1163	20011218 <--
HK	1046244	A1	20050603	HK 2002-107843	20021030 <--
US	20060134208	A1	20060622	US 2005-268500	20051108 <--
US	7410651	B2	20080812		
US	20060159749	A1	20060720	US 2006-378378	20060320 <--
US	7410652	B2	20080812		
US	20090011010	A1	20090108	US 2008-210969	20080915 <--

PRIORITY APPLN. INFO.:	IT 1999-MI1317	A	19990614 <--
	IT 2000-MI422	A	20000303 <--
	WO 2000-EP5356	W	20000609 <--
	US 2001-9532	A2	20011212 <--
	US 2005-262799	A2	20051101

AB This invention relates to controlled release and taste masking compns. containing one or more active principles incorporated in a three-component matrix structure, i.e. a structure formed by amphiphilic, lipophilic or inert matrixes and finally incorporated or dispersed in hydrophilic matrixes. The use of a plurality of systems for the control of the dissoln. of the active ingredient modulates the dissoln. rate of the active ingredient in aqueous and/or biol. fluids, thereby controlling the release kinetics in the gastrointestinal tract. For example, a taste-masked buccal tablet contained ibuprofen 100, cetyl alc. (lipophilic/inert matrix) 15, soy lecithin (amphiphilic matrix) 8, mannitol (hydrophilic matrix) 167, maltodextrin 150, hydroxypropyl Me cellulose 30, aspartame 15, flavors 5, colloidal silica 5, and Mg stearate 5 mg.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:393639 CAPLUS

DOCUMENT NUMBER: 133:114575

TITLE: A distribution study with 14C-otilonium bromide in the rat: evidence for selective tropism for large intestine after oral administration

AUTHOR(S): Evangelista, Stefano; Cochet, Pascal; Bromet, Norbert; Criscuoli, Marco; Maggi, Carlo Alberto

CORPORATE SOURCE: Menarini Ricerche S.P.A., Florence, 50131, Italy

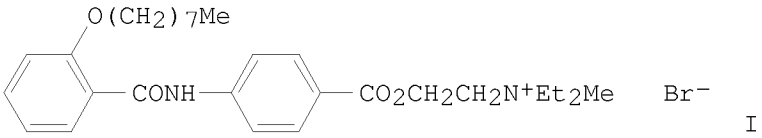
SOURCE: Drug Metabolism and Disposition (2000), 28(6), 643-647
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to determine the plasma levels and the tissue distribution of otilonium bromide, measured as total radioactivity, after oral administration of 2 mg/kg of 14C-labeled drug to rats. Radioactivity levels were very low in the plasma (ranging from 2.7 ng Eq/mL at 1.5 h to 0.6 ng Eq/mL at 24 h) as compared with those found in the gastrointestinal (GI) tract, indicating negligible systemic otilonium bromide absorption. Results from both quant. radioluminog. of whole body tissue distribution and radioassay of dissected parts of the GI tract carried out with liquid scintillation counting clearly demonstrate the presence of radioactive compds. in the walls of the GI tract at all sacrifice times. In the other tissues and organs examined, radioactivity was only found in trace amts. in the liver. The presence of radioactivity in the GI walls reflected the transit kinetics of drug-enriched contents. The radioactivity in large intestine walls was measurable at otilonium bromide concns. in the range of micromole equivalent/kg, from 4 to 8 h after drug administration. Total body radioactivity recovery was 95, 101, 24, and 9% at 1.5, 4, 8, and 24 h, resp. In conclusion, orally administered 14C-otilonium bromide is poorly absorbed systemically, as indicated by the very low plasma radioactivity levels, but it is able to effectively penetrate into the large intestine walls, a recognized target for drugs oriented toward irritable bowel syndrome therapy.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:553179 CAPLUS
DOCUMENT NUMBER: 129:310343
ORIGINAL REFERENCE NO.: 129:63161a,63164a
TITLE: Receptor binding profile of otilonium bromide
AUTHOR(S): Evangelista, Stefano; Giachetti, Antonio; Chapelain, Beatrice; Neliat, Gervais; Maggi, Carlo Alberto
CORPORATE SOURCE: Menarini Ricerche S.P.A., Florence, 50131, Italy
SOURCE: Pharmacological Research (1998), 38(2), 111-117
CODEN: PHMREP; ISSN: 1043-6618
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction of otilonium bromide (OB) with binding sites for 63 different receptors and ion channels in appropriate prepns. has been investigated. Expts. were also performed in rat colon, the preferred tissue for OB "in vivo" uptake after oral administration. Among the receptors investigated OB binds with sub μM affinity to muscarinic M1, M2, M4, M5 and PAF receptors and with μM affinity to the diltiazem binding site on L type Ca2+ channels. In the rat colon OB shows competitive interaction with the verapamil binding site on L type Ca2+ channels and with muscarinic M2 receptors with IC50 of 1020 and 1220 nM, resp. These findings provide a mol. rationale to explain the spasmolytic action exerted by OB on intestinal smooth muscle. In particular, a combination of antimuscarinic and Ca2+ channel blocker properties seems to best account for the action of this compound (c) 1998 The Italian Pharmacological Society.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1984:563101 CAPLUS
DOCUMENT NUMBER: 101:163101

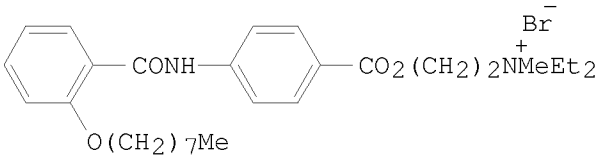
ORIGINAL REFERENCE NO.: 101:24506h,24507a
TITLE: A study of the absorption of octylonium bromide following oral administration in man
AUTHOR(S): Signorini, C.; Tosoni, S.; Ballerini, R.; Chinol, M.; Mannucci, C.
CORPORATE SOURCE: Fac. Med., Inst. Chem., Brescia, Italy
SOURCE: Drugs under Experimental and Clinical Research (1984), 10(4), 273-6
CODEN: DECRDP; ISSN: 0378-6501
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A sensitive method (10 μg/L) for the determination of octylonium bromide (I) [26095-59-0] in plasma is described. Plasma samples from healthy volunteers following oral administration of octylonium bromide (40 mg) were analyzed by gas chromatog./mass fragmentog. Under the exptl. conditions described, no plasma concns. of octylonium bromide higher than 10 μg/L were found.

L21 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1980:437410 CAPLUS
DOCUMENT NUMBER: 93:37410
ORIGINAL REFERENCE NO.: 93:6065a,6068a
TITLE: Effects of otilonium bromide on the gastrointestinal tract in vivo
AUTHOR(S): Scarpignato, C.; Coruzzi, G.; Zappia, L.; Bertaccini, G.
CORPORATE SOURCE: Ist. Farmacol., Univ. Parma, Parma, Italy
SOURCE: Farmaco, Edizione Pratica (1980), 35(5), 249-57
CODEN: FRPPAO; ISSN: 0430-0912
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI



I

AB Otilonium bromide (I) [26095-59-0] did not inhibit either basal or stimulated gastric secretion in dogs, cats, or rabbits, but it did have a spasmolytic action on the guinea pig gallbladder, the dog jejunum, and the rat pyloric sphincter; there were differences in the sensitivity of the various tissues to I. After i.p., but not oral,

administration, I relaxed the rat stomach, with consequent delay in gastric emptying. With the exception of the latter effect, which was probably through an anticholinergic mechanism, the spasmolytic activity of I appeared to be directly muscle-relaxant in nature.

L21 ANSWER 7 OF 30 MEDLINE on STN
ACCESSION NUMBER: 1986233596 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3714757
TITLE: [Clinical and instrumental evaluation by multiple colonic manometry of tiropramide, trimebutine and octylonium bromide in irritable colon. II. Repeated oral administration]. Valutazione clinica e strumentale per manometria colonica multipla di tiropramide, trimebutina ed ottilonio bromuro in pazienti con colon irritabile. II. Somministrazione ripetuta per via orale.
AUTHOR: Galeone M; Benazzi E; Bossi M; Moise G; Riva A; Stock F
SOURCE: Pharmatherapeutica, (1986) Vol. 4, No. 8, pp. 496-509.
Journal code: 7606274. ISSN: 0308-051X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198607
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 9 Jul 1986

AB Sixty out-patients with acute or sub-acute irritable colon were randomly allocated to receive 3 daily doses of 100 mg tiropramide, 150 mg trimebutine maleate or 20 mg octilonium bromide, orally during 5 consecutive days. Before and after treatment, multiple colonic manometry was performed, monitoring tonus, intensity and frequency of sinusoid contraction waves, transitories and vibrations, as well as the voluntary contraction capacity. Before treatment and after 2 and 5 days, the specific symptoms were also monitored, scored and recorded. Significant variations in tonus were not observed with any drug, but while tiropramide left unmodified the voluntary contractile ability, a significant inhibition was observed with trimebutine and, mainly, with octilonium. The overall power of spontaneous colonic contractions did not vary significantly with any drug. However, while with tiropramide a significant redistribution of muscular power was observed so as to increase propulsion waves and to decrease the ineffective transitory and vibrational contractions, with octilonium and trimebutine no clinically relevant redistribution of the power wasted in transient spasms was observed. Based on these observations, tiropramide was considered to be at least as effective an antispasmodic as octilonium and at least as effective a synchronizer as trimebutine, but was different from both reference drugs because it was the only one to act simultanously as both an antispasmodic and a synchronizer. The three drugs produced an improvement in each and all monitored symptoms as well as in the overall symptom intensity. Tiropramide, however, produced an improvement significantly faster, more progressively and to a greater extent than either reference drug.(ABSTRACT TRUNCATED AT 250 WORDS)

L21 ANSWER 8 OF 30 MEDLINE on STN
ACCESSION NUMBER: 1986177926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3960945

TITLE: [Clinical and instrumental evaluation by multiple colonic manometry of tiropramide, trimebutine and octylonium bromide in the irritable colon: I. Administration by single i.v]. Valutazione clinica e strumentale per manometria colonica multipla di tiropramide, trimebutina ed ottilonio bromuro in pazienti con colon irritabile: I. Somministrazione in dose singola i.v.
AUTHOR: Galeone M; Stock F; Moise G; Cacioli D; Benazzi E; Riva A
SOURCE: Pharmatherapeutica, (1986) Vol. 4, No. 7, pp. 445-56.
Journal code: 7606274. ISSN: 0308-051X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 25 Apr 1986

AB Sixty out-patients with acute or sub-acute irritable colon were randomly allocated to receive a single intravenous dose of 50 mg tiropramide, 50 mg trimebutine maleate or 10 mg octilonium bromide. Before and after injection, multiple colonic manometry was performed, monitoring tonus, intensity and frequency of sinusoid contraction waves, transitories and vibrations, as well as the voluntary contraction capacity. Significant variations in tonus were not observed with any drug, but, while tiropramide left unmodified the voluntary contractile ability, a significant inhibition was observed with trimebutine and octilonium. The overall power of spontaneous colonic contractions did not vary significantly with tiropramide, whereas some decrease was observed with trimebutine, and a substantial one with octilonium. Moreover, while with tiropramide and, to a lesser extent, with trimebutine there was a significant redistribution of muscular power so as to increase phasic propulsion waves and to decrease the ineffective transitory and vibrational contractions, with octilonium only a decreased wave amplitude was recorded without alteration of the frequency of transient spasms. Based on these observations, tiropramide was evaluated as being at least as effective an antispasmodic as octilonium and at least as effective a synchronizer as trimebutine, while setting itself aside from both reference drugs as it was the only one to act contemporarily as both an antispasmodic and a synchronizer.

L21 ANSWER 9 OF 30 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1992:52544 BIOSIS
DOCUMENT NUMBER: PREV199293032519; BA93:32519
TITLE: PLASMA PHARMACOKINETICS OF 300 MG OF OCTYLONIUM BROMIDE SOLUTION AFTER ENDOSCOPIC APPLICATION.
AUTHOR(S): CAPURSO L [Reprint author]; TARQUINI M; CASINI A; FORMICA N; MANNUCCI C; PERICO A
CORPORATE SOURCE: GASTROENTEROL UNIT, S FILIPPO NERI HOSP, ROME, ITALY
SOURCE: Current Therapeutic Research, (1991) Vol. 50, No. 4, pp. 539-545.
CODEN: CTCEA9. ISSN: 0011-393X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 13 Jan 1992

Last Updated on STN: 13 Mar 1992

AB Octylonium bromide (OB) is a drug with myolytic properties, which acts selectively on the smooth muscle of the gastrointestinal tract by interference with mobilization of calcium from intra- and extracellular pools. In the present study we evaluated the degree of absorption of OB, after local endoscopic application of 300 mg, by assaying the plasma levels reached after 30 minutes and after 1, 2, and 4 hours. We thus found that the peak OB plasma concentartion was reached after the first hour, whereas after four hours most patients presented very low or unassayable levels of the drug. The study confirms that OB solution, when applied locally to the colon in the course of endoscopic investigations or operations, is only slightly absorbed and is found in low plasma concentrations, comparable to those reached after oral administration.

L21 ANSWER 10 OF 30 EMBASE

ACCESSION NUMBER: 2002425849 EMBASE

TITLE: Single-dose oral tolerance test with alternative compounds for the management of adverse reactions to drugs.

AUTHOR: Passalacqua, Giovanni, Dr. (correspondence); Milanese, Manlio; Mincarini, Marcello; Ciprandi, Giorgio; Guerra, Laura; Scordamaglia, Antonio; Canonica, Giorgio Walter

CORPORATE SOURCE: Allergy and Respiratory Dis. - DIMI, Padiglione Maragliano, Largo R.Benzi 10, I-16132 Genoa, Italy. giovanni.passalacqua@hsanmartino.liguria.it

SOURCE: International Archives of Allergy and Immunology, (2002) Vol. 129, No. 3, pp. 242-247.
Refs: 28
ISSN: 1018-2438 CODEN: IAAIEG

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 5 Dec 2002
Last Updated on STN: 5 Dec 2002

AB Background: Adverse reactions to drugs are common in the clinical practice. Many outpatients are frequently referred to allergists in order to determine which drugs they can safely take in the future. Objective: We set up an oral single-dose tolerance test procedure to find out for each patient one or more alternative drugs that can be taken when needed. Methods: 452 outpatients (130 male, 322 female) with well-documented reactions (urticaria/angioedema, respiratory symptoms, laryngeal edema, anaphylaxis, exfoliative skin diseases) underwent the challenge. All tests were preceded by a single-blind placebo: if a reaction occurred, a second placebo was administered. Otherwise, a single dose (1/10 of the therapeutic one) of an alternative drug was given blindly and the patient was then observed for 6 h. The drugs used were different in structure from those suspected of having caused the adverse reaction. The patients were followed up at 4- to 6-month intervals, in order to detect any reaction that may have occurred with the tested drugs. Results: 98 patients (89 women) had untoward reactions after the first placebo and 34 out of them reacted to the second placebo, too. During challenges the reaction rate ranged between 4.6 and 9.0%; these reactions were easily managed and none of them was severe. We followed up 407 patients: 87.2% of them were able to use one or more of the suggested drugs without reactions, 9.3% did not take the drugs and only 3.5% reported reactions to the previously tested drugs. Conclusion: The challenge procedure proved to be a simple tool for managing patients with

adverse reactions to drugs. Its safety and reliability were validated by a long-term follow-up. Copyright .COPYRGT. 2002 S. Karger AG, Basel.

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L14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1086649 CAPLUS
DOCUMENT NUMBER: 149:323003
TITLE: Increased paracellular absorption by bile salts and P-glycoprotein stimulated efflux of otilonium bromide in Caco-2 cells monolayers as a model of intestinal barrier
AUTHOR(S): Catalioto, Rose-Marie; Triolo, Antonio; Giuliani, Sandro; Altamura, Maria; Evangelista, Stefano; Maggi, Carlo Alberto
CORPORATE SOURCE: Pharmacology Department, Menarini Ricerche SpA, Florence, 50131, Italy
SOURCE: Journal of Pharmaceutical Sciences (2008), 97(9), 4087-4100
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigates the intestinal permeability of otilonium bromide, a spasmolytic drug used to treat irritable bowel syndrome, across Caco-2 cell monolayers. The amount of otilonium bromide transported was determined by high-performance liquid chromatog.-mass spectrometry. Epithelial barrier integrity was estimated by measuring transepithelial elec. resistance and the transport of reference compds., P-glycoprotein activity by measuring rhodamine 123 efflux. Results showed that the apparent permeability of otilonium bromide was comparable to that of our zero permeability marker, inulin, in the apical-to-basal direction and similar to that of rhodamine 123 in the basal-to-apical direction. The P-glycoprotein substrate, verapamil, prevented otilonium bromide efflux and, conversely, otilonium bromide inhibited P-glycoprotein activity. Bile salts induced a transient opening of tight junctions, as measured by selective increase of paracellular transport, and significantly enhanced the absorption of otilonium bromide. In turn otilonium bromide potentiates the effect of bile salts on tight junctions without modifying their critical micellar concentration or altering cell viability. In conclusion, otilonium bromide is a paracellularly transported drug whose absorption, in amts. sufficient to exert a spasmolytic effect, is favored by bile salts. P-glycoprotein, by stimulating efflux, contributes to remove excess compound, restraining its distribution and site of action to the intestinal wall.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:80493 CAPLUS
DOCUMENT NUMBER: 140:122743
TITLE: P-glycoprotein inhibitor comprising octilonium bromide as an effective ingredient
INVENTOR(S): Chung, Hesson; Jeong, Seo-young; Kwon, Ick-chan; Park, Yeong-taek; Lee, In-hyun; Yuk, Soon-hong
PATENT ASSIGNEE(S): Korea Institute of Science and Technology, S. Korea
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009073	A1	20040129	WO 2003-KR1441	20030721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2004009018	A	20040131	KR 2002-42794	20020720
AU 2003281468	A1	20040209	AU 2003-281468	20030721
EP 1545495	A1	20050629	EP 2003-741600	20030721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060141033	A1	20060629	US 2005-521678	20050902

PRIORITY APPLN. INFO.: KR 2002-42794 A 20020720
WO 2003-KR1441 W 20030721

AB The invention relates to a new use of octylonium bromide as p-glycoprotein inhibitor to increase cellular uptake of drugs. More particularly, the invention provides octylonium bromide as a p-glycoprotein inhibitor to increase cellular uptake of drugs such as anticancer drugs by taking octylonium bromide simultaneously with or proceeding drug administration.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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